REMARKS

This paper is submitted in response to the Office Action mailed August 24, 2004. Claims 21-37 are pending. Claims 21, 23, 24, 27, 29-31 and 33-37 are allowable. Claims 22, 25, 28, and 32 are rejected. The claims are amended to correct inadvertent errors in grammar and spelling, so that the amendments do not constitute new matter.

The Rejections under 35 U.S.C. § 112, ¶1 Should Be Withdrawn

Claims 22, 25, 28, and 32 are rejected under 35 U.S.C. §112, first paragraph, because the specification is allegedly not enabling for a method for identifying a compound capable of modulating polycystin-1 mediated cell adherence, apical expression of NaK-ATPase, and b2NaK-ATPase, where the cell expresses a mutant polycystin-1 protein. The Examiner alleges that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Examiner alleges that the specification provides insufficient guidance as to which of the myriad of variant polypeptides will retain the characteristics of a polycystin protein and that the specification lacks detailed information regarding the structural and functional requirements of mutant polycystin-1 polypeptides. The Examiner further alleges that the specification provides only teachings on how to test for polypeptide variants of mutant polycystin-1 protein and has not taught how to make the polypeptide variants of mutant polycystin-1 protein. Therefore, the Examiner concludes that it would require undue experimentation for one of skill in the art to practice the claimed method.

Applicants respectfully traverse the enablement rejection. The claimed invention must be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F2d. at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988). Evaluation of undue experimentation involves, but is not limited to the following factors: breadth of the claims, nature of the invention, state of the prior art, level of one of ordinary skill, level of predictability, amount of direction provided by the inventor, existence of working examples and the quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F2d. at 731, 8 USPQ2d at 1400 (Fed. Cir. 1988).

Applicants assert that the specification provides sufficient disclosure for one of skill in the art to enable one of skill in the art to make and use the invention. The specification clearly teaches that mutations in the *PKD-1* or *PKD-2* genes are associated with approximately 95% of patients diagnosed with autosomal dominant polycystic kidney disease (specification, page 2, lines 11-12). The structure of wild-type polycystin-1 encoded by the *PKD-1* gene is described, with a discussion of the structural and predicted functional features of the protein (specification, page 3, lines 3-18).

The specification also describes features shared by all *PKD-1* mutants (specification, page 4, lines 8-13). In fact, the specification clearly indicates that the mutants are either truncation mutants, lacking portions of the C terminal domain or SH2 site, or mutants that result in reduced expression of β2 subunit of NaK-ATPase. In addition, example 6.2.4 show reduced tyrosine phosphorylation of the polycystin-1 protein is associated with ADPKD epithelial cells (specification, page 40, line 10 to page 41, line 4). The specification indicates that this data is consistent with polycystin-1 mutations that have been reported as deletions, missense or truncation mutants due to introduction of premature stop codons. Therefore, in contrast to the

Examiner's allegations, the specification contains specific teachings of the characteristics of mutant forms of polycystin-1.

The specification also cites to references which expressly disclose specific polycystin-1 mutants, e.g. Peral et al. at page 4 , line 13, which was provided to the Examiner with an Information Disclosure Statement mailed February 11, 2002. Peral et al., for example, identified thirteen *PKD-1* mutants, but also describe previously identified *PKD-1* mutations (Figure 6; pp. 93-95). Note that all references cited in the specification, including Peral, are incorporated by reference in their entireties at page 41, lines 5-6 of the specification.

In addition to Peral, Applicants invite the Examiner's attention to the following additional references (also listed on the accompanying PTO-1449 form), which relate to PKD-1 mutants and which were available prior to the filing date of the instant application:

Peral et al., 1995, "Splicing mutations of the polycystic kidney disease 1 (PKD1) gene induced by intronic deletion," Human Molec. Genet. 4:569-574;

The European Polycystic Kidney Disease Consortium, 1994, "The polycystic kidney disease 1 gene encodes a 14kb transcript and lies within a duplicated region on chromosome 16," Cell 77:881-894;

Watnick et al., 1997, "An unusual pattern of mutation in the duplicated portion of *PKD*1 is revealed by use of a novel strategy for mutation detection," Human Molecular Genetics 6:1473-1481;

Longa et al., 1997, "A large *TSC2* and *PKD1* gene deletion is asociated with renal and extrarenal signs of autosomal dominant polycystic kidney disease," Nephrology Dialysis Transplantation 12:1900-1907; and

Thomas et al., 1999, "Identification of mutations in the repeated part of the autosomal dominant polycystic kidney disease type 1 gene, PKD1, by long-range PCR," Am. J. Human Genetics 65:39-49.

Applicants therefore submit that the specification fully supports the breadth of claims 22, 25, 28, and 32, because it describes variants of mutant polycystin-1 protein that may be used to practice the invention, as discussed above. Given that a number of mutants had been identified in the art, and the description of the common mutant attributes of the *PKD-1* gene found in the specification, Applicants submit that undue experimentation is not required.

Furthermore, the test for enablement is whether one reasonably skilled in the art could make and use the invention from the disclosure in the patent coupled with information known in the art without undue experimentation. *U.S. v. Telectronics, Inc.* 857 F2d 778, 8 USPQ 2d 1217 (Fed. Cir 1988) cert denied, 490 U.S. 1046 (1989). A patent need not teach, and preferably omits, what is well-known in the art. *Lindemann, Maschinen fabrik GmBH v. American Hoist & Derrick Co.*, 730 F2d 1452, 221 USPQ 481 (Fed. Cir. 1984). Applicants submit that given the knowledge of the skilled artisan and the teachings of the present specification, claims 22, 25, 28, and 32 are clearly enabled.

Claims 22, 25, 28, and 32 are also rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed, had possession of the invention. The Examiner alleges that the specification does not does not describe sufficient descriptive information, such as definitive structural or functional features common to members of the genus of polypeptides. The Examiner alleges that one of

skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus.

Applicants also respectfully traverse the written description rejection. An applicant may show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. *Guidelines for Examination of Patent Application Under the 35 U.S.C., ¶1, "Written Description" Requirement.* 66 FR 1099, 1106.

The specification clearly discloses relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention. For example, the specification clearly describes multiple structural variants of mutant polycystin-1, e.g. deletions, missense or truncation mutants. The specification also teaches functional characteristics of the mutant phenotype created, i.e. increased adherence to type I collagen coated surfaces, apical expression of β2-NaK-ATPase, and decreased focal adhesion kinase incorporation into focal adhesion complexes, and inability to form tubular structures in a gel matrix (specification, abstract). In addition, the specification cites references that provide specific mutant forms of the *PKD-1* gene. Therefore, applicants submit that the specification provides sufficient detailed description to satisfy the written description requirement.

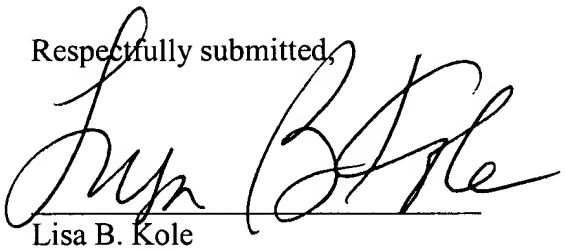
For the foregoing reasons, Applicants respectfully request withdrawal of the rejection of claims 22, 25, 28, and 32 under 35 U.S.C. §112, first paragraph.

CONCLUSION

In view of the foregoing amendments and remarks, Applicant respectfully requests withdrawal of the outstanding rejections and allowance of the pending claims.

Applicants request a three month extension of time and enclose herewith the requisite fee as set forth in 37 C.F.R. § 1.17(a)(3). Applicant does not believe that any additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,



Lisa B. Kole
Patent Office Reg. No. 35,225

BAKER BOTTS L.L.P.
30 Rockefeller Plaza
New York, New York 10112-0228

Attorney for Applicants
(212) 408-2500